

THAT WHICH IS CLAIMED IS:

1. A composition comprising a population of infectious, attenuated, alphavirus replicon particles in an immunogenically effective dosage, wherein
5 each of said alphavirus particles comprises:

(a) a virion shell comprising Venezuelan Equine Encephalitis (VEE) structural proteins, wherein said virion shell further comprises an attenuating mutation in the E1 glycoprotein;

(b) a recombinant alphavirus replicon RNA comprising a heterologous
10 nucleotide sequence encoding an immunogen, wherein said heterologous nucleotide sequence is operably associated with a promoter,

wherein said immunogenically effective dosage comprises a number of infectious alphavirus particles that is (i) substantially the same as or substantially less than the immunogenically effective dosage of a comparable alphavirus
15 having a wild-type VEE virion shell or (ii) is less than about 100-fold more than the immunogenically effective dosage of a comparable alphavirus having a wild-type VEE virion shell.

2. The composition of Claim 1, wherein said immunogenically
20 effective dosage comprises substantially the same number of infectious alphavirus particles as an immunogenically effective dosage of a comparable virus having a wild-type VEE virion shell.

3. The composition of Claim 1, wherein said immunogenically
25 effective dosage comprises a substantially lower number of infectious alphavirus particles than an immunogenically effective dosage of a comparable alphavirus having a wild-type VEE virion shell.

4. A composition comprising a population of infectious, attenuated, alphavirus replicon particles in an immunogenically effective dosage, wherein
30 each of said alphavirus particles comprises:

(a) a virion shell comprising Venezuelan Equine Encephalitis (VEE) structural proteins, wherein said virion shell further comprises an attenuating mutation in the E1 glycoprotein;

(b) a recombinant alphavirus replicon RNA comprising a heterologous nucleotide sequence encoding an immunogen,
wherein said alphavirus particles exhibit only weak or no detectable binding to heparin.

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5. The composition of any of Claims 1-4, wherein said attenuating mutation in the E1 glycoprotein comprises an attenuating mutation in the fusogenic peptide region.

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6. The composition of any of Claims 1-4, wherein said attenuating mutation in the E1 glycoprotein comprises an attenuating mutation selected from the group consisting of (i) an attenuating mutation at E1 glycoprotein amino acid position 81, and (ii) an attenuating mutation at E1 glycoprotein amino acid position 253.

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7. The composition of Claim 6, wherein said VEE virion shell comprises a Phe → Ile attenuating mutation at E1 glycoprotein amino acid position 81.

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8. The composition of Claim 6, wherein said VEE virion shell comprises a Phe → Ser attenuating mutation at E1 glycoprotein amino acid position 253.

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9. The composition of any of Claims 1-8, wherein said composition comprises about 10^2 to about 10^6 infectious alphavirus particles.

10. The composition of any of Claims 1-8, wherein said composition comprises about 10^3 to about 10^5 infectious alphavirus particles.

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11. The composition of any of Claims 1-8, wherein said composition comprises about 10^5 to about 10^9 infectious alphavirus particles.

12. The composition of Claim 11, wherein said composition comprises about 10^6 to about 10^8 infectious alphavirus particles.

13. The composition of any of Claims 1-12, wherein said recombinant alphavirus replicon RNA is a recombinant VEE replicon RNA.

5 14. The composition of any of Claims 1-13, wherein said promoter is an alphavirus 26S subgenomic promoter.

15. The composition of any of Claims 1-14, wherein said immunogen is a cancer immunogen.

10 16. The composition of any of Claims 1-14, wherein said immunogen is an infectious disease immunogen.

15 17. The composition of Claim 16, wherein said immunogen is selected from the group consisting of a bacterial immunogen, a viral immunogen, and a protozoa immunogen.

20 18. The composition of any of Claims 1-15, 17 or 18, wherein said immunogen is an Simian Immunodeficiency Virus (SIV) immunogen or a Human Immunodeficiency Virus (HIV).immunogen.

25 19. The composition of Claim 18, wherein said immunogen is a SIV or HIV immunogen selected from the group consisting of a *gag*, *env*, *ref*, *tat*, *nef* and *pol* gene product, and a combination thereof.

20. The composition of any of Claims 1-19, wherein said replicon RNA lacks sequences encoding the VEE structural proteins.

30 21. A pharmaceutical formulation comprising the composition of any of Claims 1-20 in a pharmaceutically acceptable carrier.

22. A method of producing an immune response in a subject, comprising administering to the subject an immunogenically effective amount

of a composition according to any of Claims 1-20 or a pharmaceutical formulation according to Claim 21.

23. A method of producing an immune response in a subject,
5 comprising:

(a) administering *ex vivo* to a plurality of cells a composition according to any of Claims 1-20 or a pharmaceutical formulation according to Claim 21, and

(b) administering an immunogenically effective amount of the cells
10 to the subject.

24. The method of Claim 23, wherein the plurality of cells comprises dendritic cells.

15 25. The method of any of Claims 22-24, wherein a protective immune response is induced in the subject.

26. The method of Claim 22, wherein said administering step is carried out by subcutaneous administration.
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27. The method of Claim 22, wherein said administering step is carried out by intradermal administration.

28. The method of any of Claims 22, or 25-27, wherein said
25 administering step is carried out by administration to a limb of the subject.

29. The method of Claim 28, wherein said administering step is to a front limb of the subject.

30 30. The method of any of Claims 22-29, wherein the subject is a mammalian subject.

31. The method of Claim 30, wherein the subject is selected from the group consisting of a primate subject, a pig, a cow, a dog and a cat.

32. The method of Claim 31, wherein the subject is a human subject.

33. The method of Claim 32, wherein the subject has, or is at risk of
5 developing, AIDS.

34. The method of Claim 24, wherein the heterologous nucleotide
sequence is introduced into the dendritic cells and the dendritic cells express
the immunogen.
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35. The method of Claim 24 or Claim 34, wherein said contacting
step is carried out *in vitro*.

36. The method according to Claim 34 or Claim 34, wherein said
15 contacting step is carried out *in vivo*.